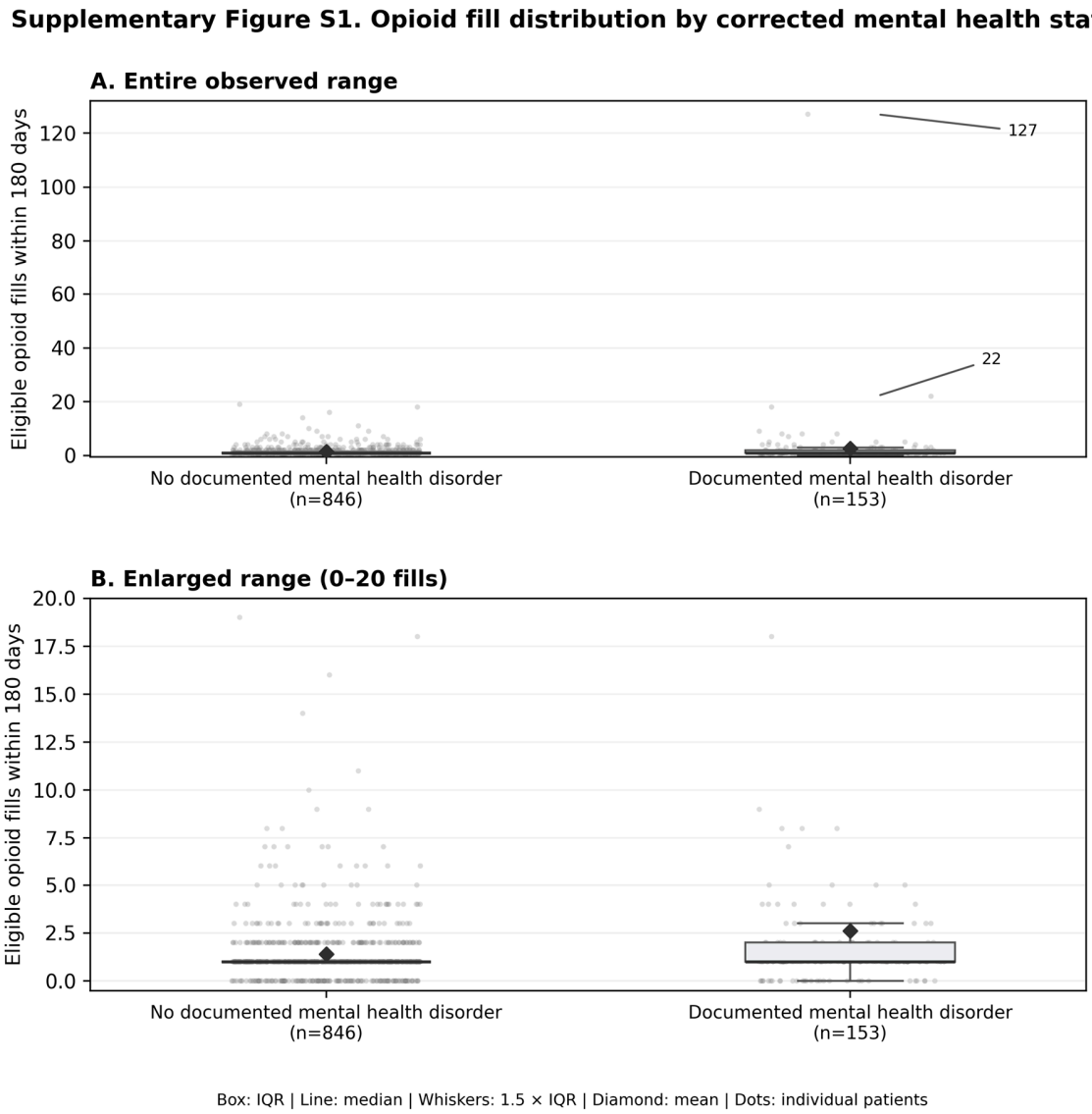
Supplementary Materials

Documented Mental Health Disorders and Long-Term Opioid Therapy After Hospital Discharge in a Predominantly Cardiothoracic Surgical Cohort

Figure S1. Distribution of outpatient opioid fills within 180 days by documented mental health disorder status.



Panel A shows the complete observed range, including 22 and 127 fills; panel B magnifies counts from 0 to 20. Boxes represent interquartile ranges; horizontal center lines, medians; whiskers, observations within 1.5 × IQR; diamonds, means; points, individual patients. Both extreme observations are displayed in panel A but lie outside panel B. The 127-fill observation was retained in the full-cohort secondary fill-rate estimate; the retained dispensing extract contained distinct records by product identifier and dispensing date, although the underlying pharmacy transactions were not independently adjudicated. Group sizes were n=846 without and n=153 with a documented mental health disorder; two extreme fill-count observations (22 and 127) remain within the exposed group.

Table S1. Descriptive opioid-dispensing outcomes by mental health disorder status.

Group	N	Any opioid fill	Mean opioid days (median)	Mean fills (median)	≥5 fills	≥10 fills	≥20 fills	≥90 days
No documented mental health disorder	846	700 (82.74%)	11.39 (5)	1.39 (1)	33 (3.90%)	6 (0.71%)	0 (0.00%)	12 (1.42%)
Documented mental health disorder	153	124 (81.05%)	14.01 (6)	2.61 (1)	12 (7.84%)	3 (1.96%)	2 (1.31%)	2 (1.31%)

Days supplied were calculated with patient-level carry-forward and capped at discharge day 179. Percentages use group denominators. The 14 LTOT events comprise 12 without and two with documented mental health disorders.

Table S2. Opioid product eligibility at discharge, baseline, and follow-up.

Source drug or listing	Study eligibility by analytic stage
Oxycodone (N02AA05)	Eligible for new discharge prescribing, baseline opioid look-back and follow-up outcome; 799 newly prescribed at discharge.
Hydromorphone (N02AA03)	Eligible at all three stages; 185 newly prescribed at discharge.
Morphine (N02AA01)	Eligible at all three stages; 20 newly prescribed at discharge.
Codeine + acetaminophen (N02AJ06)	Eligible combination product at all three stages; 1 newly prescribed at discharge.
Transdermal fentanyl (N02AB03)	Flagged in intermediate dispensing extract but excluded by the operational rule at baseline and follow-up; none newly eligible at discharge.
Single-ingredient codeine (R05DA04)	Flagged in intermediate dispensing extract but excluded by the operational rule at baseline and follow-up.
Methadone (N07BC02)	Flagged in intermediate dispensing extract but excluded by the operational rule at baseline and follow-up.
Other ATC opioid classes / examples	Tramadol, tapentadol, hydrocodone, and related ATC-listed analgesics are pharmacological examples, not additional qualifying products under the restricted study rule.

The claims-selection extract flagged oxycodone, hydromorphone, morphine, codeine–acetaminophen, transdermal fentanyl, single-ingredient codeine, and methadone. Only the first four drug-name categories met the restricted operational definition at discharge, baseline, and follow-up; these were also the only newly prescribed eligible discharge products. Anatomical Therapeutic Chemical (ATC) codes describe products but do not independently establish eligibility. Tramadol, tapentadol, hydrocodone, and other ATC examples did not enter the restricted study algorithm. These restrictions may omit clinically meaningful opioid treatment and are assessed in Tables S12–S13. Clinical indication was not adjudicated.

Table S3. Documented mental health diagnostic-category distribution.

Category (not mutually exclusive)	n	% among 153
Anxiety disorder	71	46.4
Depressive disorder	36	23.5
Adjustment disorder	25	16.3
Addictive disorder	12	7.8
Delirium/confusion	14	9.2
Psychotic disorder	11	7.2
Neurotic disorder	11	7.2
Miscellaneous mental health disorder	9	5.9
Bipolar disorder	6	3.9
Neurodevelopmental disorder	3	2.0
Trauma-related disorder	2	1.3
Personality disorder	2	1.3
Suicidal ideation/attempt indicator	2	1.3
Obsessive-compulsive disorder	0	0.0
Eating disorder	0	0.0

Under the corrected exposure algorithm, 116/153 (75.8%) had one category and 37/153 (24.2%) had two or more. Diagnostic categories are not mutually exclusive. The source algorithm was preserved except for removing ICD-9 2898 from psychosis and ICD-10 V654 from addiction; corresponding classification effects are shown in Table S11.

Table S4. Primary and exploratory outcome/ascertainment definitions.

Analysis	Events (MH/no MH when applicable)	Adjusted MH association
Primary ≥90 days patient-level carry-forward	14 (2 / 12)	Firth OR 1.07 (0.20–3.73)
Diagnosis ascertainment through discharge	14 (2/12); MH n=150	Firth OR 1.09 (0.21–3.78)
Clinical-service adjustment	14 (2 / 12)	Firth OR 1.02 (0.19–3.60)
Molecule-specific carry-forward + calendar union	13 (2 / 11)	Not fitted
Distinct observed calendar days without stockpiling	9 (2 / 7)	Not fitted
Influence refit: remove maximum 127 fills	Not an LTOT sensitivity	Fill rate ratio 1.22 (1.04–1.44)
Influence refit: remove both ≥20-fill observations	Not an LTOT sensitivity	Fill rate ratio 1.14 (0.97–1.35)
Exclude three participants with interview-status death flag (date unknown)	14 (2 / 12); N = 996; MH n = 156	Initial-definition Firth OR 1.04 (0.20–3.63)

MH = corrected documented mental health disorder except where explicitly labelled "initial definition"; LTOT = long-term opioid therapy; OR = odds ratio; CI = confidence interval. Exposure-correction models and ancillary outcomes are reported in Tables S11–S13. Overlap algorithms use different exposure assumptions. The historical death-status sensitivity is retained for context; it cannot establish death timing or competing risks. All intervals are patient-level and do not account for intra-unit correlation.

Table S5. Operational ICD-9/ICD-10 diagnostic-category algorithms and separate SMI indicator.

The code rules below reflect the corrected primary diagnostic classification. D represents the complete recorded diagnosis string and X its first three characters; D IN (...) is an exact match, whereas X IN (...) or X = ... is a prefix match. The source code mappings and their corrections are compared in Table S11. These operational rules have not been externally validated for this study.

Diagnostic category	SAS indicator	Exact operational diagnosis-code rule
Depressive Disorders	depressive_disorder	(d in ('3119','3091','3090','3004','2980','2961','F329') or x='311')
Anxiety Disorders	anxiety_disorder	D in ('3000','3002','3130','F419','F411','F938')
Bipolar Disorders	bipolar_disorder	D in ('2960','2962','2961','2963','2964','2965','2966','2967','F31')
Psychotic Disorders	psychotic_disorder	(D in ('2911','2912','2913','2914','2915','2918','2919', '2941','2948','2949','2971','2972','2978','2979', '2990','2991','2968','2969','F209') OR X in ('292','295','F20','F21'))
Delirium/Confusion Disorders	delirium_disorder	(D in ('2982') OR X in ('293'))
Trauma-Related Disorders	trauma_disorder	d in ('3081','3082','3080','3083','3084','3089','F431')
Obsessive-Compulsive Disorder	obsessive_compulsive_disorder	d in ('3003')
Eating Disorders	eating_disorder	d in ('F500','3071','3075')
Neurodevelopmental Disorders	neurodevelop_disorder	d in ('3140','3180','F840','F900')
Addictive Disorders	addictive_disorder	(d in ('3030','3039','3094','3057','3575','4225','5353','5711','5712','5713', '6483','9650','9685','9696','F102') OR X IN ('304','305','F10','F11','F12','F19'))
Personality Disorders	personality_disorder	(d in ('F603','F602') OR X='301')
Neurotic Disorders	neurotic_disorder	d in ('3005','3007','3008','3009')
Adjustment Disorders	adjustment_disorder	(d in ('3091','3092','3093','3094','3098','3099','3090','F432') OR X='309')
Miscellaneous Disorders	miscellaneous_disorder	d in ('3028','3029','3063','3065','3069','3070','3074','3078','3079','3100','3101','3109','3129','3139')
Suicidal ideation/attempt	Suicidal_attempt	(d in ('V628','T1419','Z915')or x='E92')

The primary classification excludes ICD-9 2898 from the psychotic-disorder rule and ICD-10 V654 from the addictive-disorder rule. All other operational diagnostic-category rules were retained. The separate SMI descriptor excludes the ICD-9 293 delirium prefix, giving 15 SMI-positive patients. Table S11 documents the source-versus-corrected classification and sensitivity analyses.

Separate serious mental illness (SMI) rule

Separate SMI operational rule (not simply bipolar OR psychotic): (d in ('2950','2951','2952','2953','2956','2957','2958','2959','2960', '2962','2961','2963','2964','2965','2966','2967', '2966','2967','2968','2971','2972','2978','2979','2980','2982','2988','F323','F333') or x IN ('F20', 'F22', 'F23', 'F25', 'F28','F29', 'F30', 'F31','F21'))

Coding note: D refers to the full diagnosis string, and X to its first three characters; D matches are exact and X matches are prefixes. At least one qualifying diagnosis defines the composite mental-health exposure, and category indicators are not mutually exclusive. The rules in Table S5 represent the corrected primary classification (n=153); initial mappings and their patient-level effects, including the distinct delirium-exclusion analysis, appear in Table S11. The code-based categories have not been clinically adjudicated.

Table S6. LTOT by admitting clinical service and documented mental health disorder.

Service	Documented MH	Patients	LTOT events	LTOT %
Cardiothoracic surgery	No	790	8	1.01%
Cardiothoracic surgery	Yes	136	1	0.74%
Internal medicine	No	56	4	7.14%
Internal medicine	Yes	17	1	5.88%

The source grouped the two relevant surgical trial units under "Cardiac Surgery"; the parent RightRx report distinguishes cardiac and thoracic units. We use "cardiothoracic surgery" consistently for this combined group. These are descriptive rates and are not separate powered comparisons. LTOT = long-term opioid therapy; MH = corrected documented mental health disorder.

Table S7. Molecules newly prescribed at discharge by documented mental health disorder status.

New opioid recorded	No documented MH (n=846)	Documented MH (n=153)	Total patients
Oxycodone	686 (81.1%)	113 (73.9%)	799
Hydromorphone	147 (17.4%)	38 (24.8%)	185
Morphine	18 (2.1%)	2 (1.3%)	20
Codeine + Acetaminophen	1 (0.1%)	0 (0.0%)	1

Drug groups are not mutually exclusive because some patients were prescribed more than one new opioid. Dose, quantity, and duration fields were incomplete and derived from nonidentical control and intervention data sources. They were therefore not pooled to calculate a supposedly comparable full-cohort morphine-equivalent dose or initial days supplied.

Table S8. Exploratory LTOT counts by randomized intervention assignment and documented mental health disorder.

Randomized assignment	Documented MH	N	LTOT events, n (%)
Usual care	No	396	10 (2.53%)
Usual care	Yes	82	2 (2.44%)
Electronic reconciliation intervention	No	450	2 (0.44%)
Electronic reconciliation intervention	Yes	71	0 (0.00%)

MH = corrected documented mental health disorder. LTOT = ≥90 modeled opioid days on days 0–179. Four randomized study units contributed, not four independent treatment arms; the distribution is descriptive, not a valid effect-modification test. No exposure-by-intervention interaction estimate is presented for the corrected classification.

Table S9. Additional exploratory secondary outcome sensitivity models.

Post hoc analysis	Excluded patients	Adjusted rate ratio (95% CI)	Nominal p-value
Opioid fills: exclude ≥10 fills	9	1.17 (1.00–1.36)	0.0470
Opioid fills: exclude LTOT	14	1.25 (1.07–1.46)	0.0047
Opioid days: exclude LTOT	14	1.13 (0.92–1.40)	0.2413
Opioid days: exclude ≥120 supplied days	6	1.04 (0.84–1.29)	0.7105

Models were refitted using the corrected n=153 exposure, adjusting for age, sex and trial arm. Nominal p-values were not corrected for multiplicity. Restrictions are outcome-dependent exploratory diagnostics and must not supersede the original full-sample analysis. Confidence intervals do not account for within-unit correlation.

Table S10. Short-term hospitalization and mortality-status fields available in the RightRx parent-trial extract.

Extracted indicator	Value in the 999-person cohort	Interpretation / limitation
Original parent trial participant records	3,567	Unique patient identifiers in parent research extract; 999 linked to final analytic cohort
Any hospitalization by day 30	74 / 999 (7.4%)	TRUE_HOSP_30a field; precomputed study flag
Any hospitalization by day 60	103 / 999 (10.3%)	TRUE_HOSP_60a field; precomputed study flag
Any hospitalization by day 90	124 / 999 (12.4%)	TRUE_HOSP_90a field; precomputed study flag
30-day death flag	5 / 999 (0.5%)	death_30d field; unvalidated in supplied extracts
Interview status labeled Death	3 / 999 (0.3%)	STATUS_INTERW; overlaps with the five flagged deaths
Recorded non-placeholder death date	2 / 999 (0.2%)	date1DEATH; both recorded one day after index discharge
Complete 180-day outpatient drug eligibility	Not established	No complete enrollment or termination date series supplied
Complete 180-day death/readmission time series	Not established	Short-term study indicators cannot reconstruct all days 0–179

Notes. Hospitalization indicators (TRUE_HOSP_30a/60a/90a) and death/status variables were derived in earlier RightRx trial analyses and were not independently validated here. Their categories may overlap and must not be summed. The three interview-status deaths are included among the five 30-day death flags. A separate death-status extract contained no death dates, whereas the parent-trial patient extract included two non-placeholder date1DEATH values. Recorded dates and flags do not establish complete 180-day survival or pharmacy claims eligibility. The 2,544-person discharge-prescribing source is a curated subset of the 3,567-patient parent trial, but the upstream 1,023 exclusions/linkage losses cannot be reconstructed from the available source records.

Table S11. Diagnostic-code classification corrections and sensitivity estimates.

Finding or model	Historical definition	Corrected definition / impact
ICD-9 2898 mapped to psychosis	Two exclusive exposed patients	Removed (source label: blood disorder)
ICD-10 V654 mapped to addiction	Two exclusive exposed patients	Removed (source label: transport accident)
ICD-9 E92 suicidality prefix	No affected patients	Potentially nonspecific; no change in 999 cohort
ICD-9 3051 tobacco	Two code-positive patients	Retained in corrected composite; optional narrow-addiction sensitivity n=152, adjusted LTOT OR 1.08 (0.21–3.76).
ICD-9 2961/2962/2963 and ICD-10 F31/F32/F33	Mood-code overlap or exact-prefix issues	No patient-level reclassification under verified source data; retain and disclose
Delirium/confusion category	14 category-positive; 8 delirium-only	Excluding delirium changes MH n=153 to 145; 2 LTOT events retained
Serious mental illness descriptor	23 source-positive including ICD-9 293	15 after excluding ICD-9 293 delirium prefix
Corrected MH composite size	157 (15.7%)	153 (15.3%); four reclassified to no MH
Primary LTOT, adjusted Firth OR (95% CI)	1.04 (0.20–3.62)	1.07 (0.20–3.73); 14 events (2/12) unchanged
Any opioid dispensing, adjusted RR	0.99 (0.91–1.07)	0.98 (0.91–1.07)
Number of opioid fills, adjusted NB rate ratio	1.50 (1.26–1.78)	1.51 (1.27–1.79)
Days supplied, adjusted NB rate ratio	1.10 (0.88–1.38)	1.09 (0.87–1.37)
Corrected MH without delirium, adjusted LTOT OR	Not in original report	1.13 (0.22–3.93); n=145; 2/14 events
Corrected MH, diagnosis by discharge only, adjusted LTOT OR	Historical 1.06 (0.20–3.67)	1.09 (0.21–3.78); n=150

Diagnostic-code classification used patient-level diagnosis strings and description labels from dated RAMQ/MOXXING medical-services records. The source classification contained two nonpsychiatric code mappings (ICD-9 2898 and ICD-10 V654); removing them reclassified four patients and defined the corrected 153-person composite. No relevant F31/F32/F33 code-family omissions or E92 cases were observed, and code-level specificity is not equivalent to clinical validation. MH = documented mental health disorder. The SAS pipeline constructed BILO from the combined medicalservices extract. The separate MED-ÉCHO index-admission diagnosis comparison matched all 999 index admissions, found that all 43 MED-ÉCHO-positive patients were among the 153 medical-services-positive participants, and identified 214 qualifying MED-ÉCHO diagnosis rows that reduced to 44 distinct patient–diagnosis-code pairs; all 44 matched in medicalservices at the patient and diagnostic-code/category level (Table S14). That comparison does not establish the clinical validity of the phenotype or complete longitudinal inpatient ascertainment. Analyses other than the designated corrected primary model are exploratory.

Table S12. Opioid product eligibility across cohort selection, baseline, and follow-up.

Operational check	Observed in retained 999 cohort	Effect / qualification
New discharge opioid product categories	Oxycodone 799; hydromorphone 185; morphine 20; codeine–acetaminophen 1 (nonexclusive)	Fentanyl patches, methadone, single-ingredient codeine not eligible as NEW discharge opioid
Excluded baseline products, days −180 to −1	10 distinct patients (one patch, seven single-ingredient codeine, two methadone)	All retained by original narrow opioid-naïve rule; none met primary LTOT
Fentanyl transdermal during follow-up	47 records in 9 patients	Excluded in original source; may represent clinically meaningful therapy
Single-ingredient codeine during follow-up	8 records in 5 patients	Excluded in original source
Methadone during follow-up	8 records in 3 patients	Excluded in original source
Original eligible product set	824 patients with follow-up dispensing	14/999 meet ≥90 modeled supplied days
Expanded product set in follow-up	Fentanyl patch + single codeine + methadone added	19/999 meet ≥90 modeled supplied days, including 4/153 corrected MH versus 15/846 without; adjusted Firth OR 1.55 (95% CI 0.46–4.26). Exploratory broadened follow-up only; discharge and baseline source eligibility unchanged.
Original LTOT after additionally excluding 10 with excluded baseline products	989 patients; 14 events	Exploratory corrected-exposure OR ≈1.08 (point estimate only)
Expanded LTOT after additionally excluding 10 with excluded baseline products	989 patients; 16 events	16/989 events, including 3/151 corrected MH versus 13/838 without; adjusted Firth OR 1.40 (95% CI 0.35–4.25). Excludes 10 patients with baseline claims for products omitted in the historical eligibility definition.

Counts reproduce the original 999-person source. Restricted opioid day counts were reconstructed exactly for all 999 patients using the verified patient-level across-molecule carry-forward routine, positive durations, distinct DIN/date/duration, and truncation to day 179. Expanded-product sensitivity is not identical to active clinical use, and baseline product exclusions may affect whether a patient is considered opioid-naïve. Results do not establish continuous RAMQ enrollment or complete follow-up. ATC categories are descriptive and are not an exhaustive eligibility list; Table S2 distinguishes included drug-name groups, excluded products, and reference-only ATC examples.

Table S13. Alternative late-dispensing outcome, source cancer flag, and clustering considerations.

Analysis or descriptive check	Value	Interpretation
Eligible fill during days 90–179	89/999 (8.9%)	18/153 with corrected MH and 71/846 without
Corrected MH association with late fill	Adjusted Firth OR 1.42 (95% CI 0.80–2.41)	Distinct, less stringent persistence definition from Brummett et al.; not primary LTOT
Historical MH association with late fill	Adjusted Firth OR 1.37 (95% CI 0.77–2.32)	For original-versus-corrected comparison
Source-derived CANCER flag	401/999 (40.1%)	333/846 without corrected MH, 68/153 with; does not confirm active cancer or opioid indication
Cancer flag by LTOT	10/14 primary LTOT events	4/598 without flag and 10/401 with flag
Cancer flag by trial arm	55/521 intervention; 346/478 usual care	Marked imbalance; not necessarily active cancer at discharge
Corrected MH primary model plus cancer flag	Adjusted OR 1.06 (95% CI 0.20–3.68)	Exploratory, sparse events; not a causal solution
Original parent trial clustering	Four randomization units (medical/surgical by hospital)	Parent trial used two-step bootstrap for randomized trial intervention effect
Corrected MH association cluster inference	Patient-level CI only	Four units, 14 events; undercoverage possible, no valid small-cluster CI claimed
Broadened LTOT, original fixed cohort	19/999; 4/153 corrected MH and 15/846 no MH; adjusted Firth OR 1.55 (0.46–4.26)	Includes fentanyl patches, single-ingredient codeine and methadone during follow-up; unchanged historical cohort selection
Broadened LTOT excluding baseline-excluded-product patients	16/989; 3/151 corrected MH and 13/838 no MH; adjusted Firth OR 1.40 (0.35–4.25)	Exploratory 10-patient baseline exclusion; no newly reconstructed opioid-naïve cohort

Models adjust for age, sex, and trial arm unless the cancer flag is specifically added. Late dispensing refers to a dated pharmacy fill on days 90–179 and does not establish continuous opioid consumption. Mental-health status was not randomized. The source CANCER flag was not clinically adjudicated as an active cancer-pain indication. The parent trial contained 3,567 unique patient IDs, including 297/1,690 CANCER-positive intervention participants and 900/1,877 CANCER-positive usual-care participants [9]. All 999 analytic patient IDs linked uniquely to this parent file, with matching trial-arm assignments. In the analytic cohort, CANCER was flagged in 55/521 intervention participants and 346/478 usual-care participants. See references [4,9,12]. The separate MED-ÉCHO index-admission diagnosis comparison is summarized in Table S14.

Table S14. MED-ÉCHO index-admission linkage and qualifying-diagnosis concordance.

Component	Result/scope
Sources and original exposure	BILO exposure derived from combined RAMQ/MOXXING medicalservices; MED-ÉCHO index-admission diagnosis records were assessed separately.
Patient-level linkage	999/999 (100%) analytic participants linked to MED-ÉCHO and corresponding parent RightRx records.
Index admission verification	999/999 (100%) index hospitalizations verified against parent RightRx admission and discharge dates.
Diagnosis-code processing	MED-ÉCHO and medicalservices ICD-9/ICD-10 strings were standardized (including punctuation). The corrected mental-health rules were applied to both sources. Repeated MED-ÉCHO diagnosis rows were deduplicated by patient and standardized code.
Diagnosis-level matching rule	Qualifying index-admission diagnoses were matched to medicalservices by patient and diagnosis code/category within the defined ascertainment window. The unit was a distinct patient–diagnosis-code pair, not a raw diagnosis row or binary exposure status.
Medical-services-positive participants	153/999 (15.3%) with corrected medicalservices-based mental-health exposure.
MED-ÉCHO index-admission-positive participants	43/999 (4.3%) had ≥1 qualifying MED-ÉCHO index-admission mental-health diagnosis.
MED-ÉCHO-positive participants also medical-services-positive	43/43 (100%) were included among the 153 medicalservices-positive patients.
MED-ÉCHO-only positive participants	0
Combined-source mental-health-positive participants	153/999 (15.3%); no change after combining sources.
Qualifying MED-ÉCHO diagnosis rows before deduplication	214 qualifying MED-ÉCHO diagnosis rows before deduplication, including repeated records; these are not the diagnosis-level denominator.
Primary LTOT results	14/999 LTOT events (2/153 exposed; 12/846 unexposed); adjusted Firth OR 1.07 (95% CI 0.20–3.73), unchanged.
Interpretive scope One-directional index-admission capture only; does not establish full longitudinal inpatient coverage, bilateral identity of all records, clinical phenotype validity, or continuous 180-day pharmacy eligibility.	